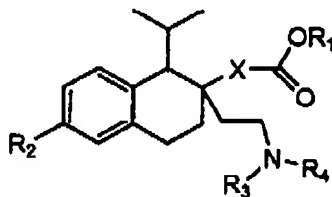


AMENDMENTS**IN THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Withdrawn) A calcium channel blocker compound having at least one of the following characteristics:
 - a. the compound is metabolized both by CYP450 and by a non-oxidative metabolic enzyme or system of enzymes;
 - b. the compound has a short (up to four (4) hours) non-oxidative metabolic half-life;
 - c. the compound contains a hydrolysable bond that can be cleaved non-oxidatively by hydrolytic enzymes;
 - d. the primary metabolites of the compound result from the non-oxidative metabolism of the compound;
 - e. the primary metabolites are soluble in water at physiological pH;
 - f. the primary metabolites have negligible inhibitory activity at the IK_R (HERG) channel at normal therapeutic concentration of the parent drug in plasma;
 - g. the compound, as well as the metabolites thereof, does not cause metabolic DDI when co-administered with other drugs; and
 - h. the compound, as well as metabolites thereof, does not elevate LFT values when administered alone.
2. (Withdrawn) The compound, according to claim 1, having the following structure:



wherein:

X=a bond, $(CH_2)_n$, O, S, or $O(CH_2)_n$,

wherein $n=1-6$;

$R_1=C_{1-6}$ alkyl, optionally substituted with OH or NH_2 ;

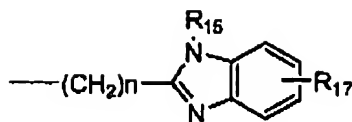
$R_2=F$ or $COOR_5$,

wherein R_5 is C_{1-6} alkyl, optionally substituted with OH or NH_2 ;

$R_3=CH_3$ or $(CH_2)_n-COOR_6$,

wherein $n=1-6$ and R_6 is C_{1-6} alkyl, optionally substituted with OH or NH_2 ;

$R_4 = (CH_2)_n - COR_7R_8$, $-(CH_2)_n - R_{10}R_{11}$ or



$R_7 = O, NH, \text{ or } NR_9$,

$R_8 = \text{optionally substituted aryl or heterocycle}$,

$R_9 = C_{1-6}$ alkyl,

$R_{10} = O, S, SO, SO_2, NH, \text{ or } NR_{12} \text{ or } N(CH_2)_m COOR_{13}$,

$R_{11} = \text{aryl or heterocyclyl optionally substituted with } (CH_2)_n COOR_{14}$,

$R_{12} = C_{1-6}$ alkyl, optionally substituted with OH or NH_2 ,

$R_{13} = C_{1-6}$ alkyl, optionally substituted with OH or NH_2 ,

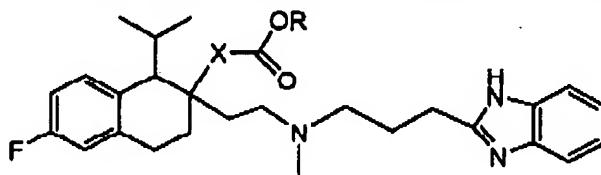
$R_{14} = C_{1-6}$ alkyl, optionally substituted with OH or NH_2 ,

$R_{15} = (CH_2)_n COOR_{16}$,

$R_{16} = C_{1-6}$ alkyl, optionally substituted with OH or NH_2 ,

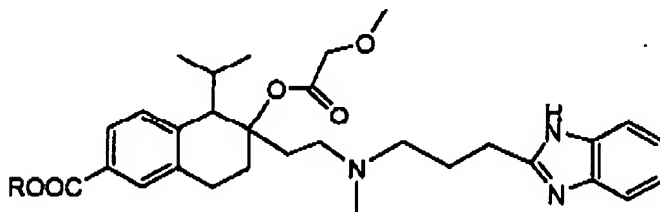
$R_{17} = \text{not present or } COOR_{18} \text{ wherein } R_{18} \text{ is } C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2, \text{ and}$
 wherein $n = 1-6$.

3. (Withdrawn) The compound, according to claim 2, having a formula selected from the group consisting of:

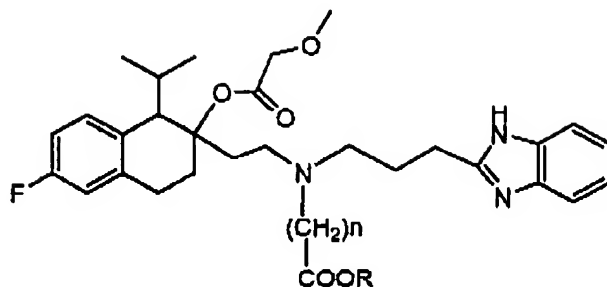


$X = \text{bond, } CH_2, \text{ or } OCH_2$

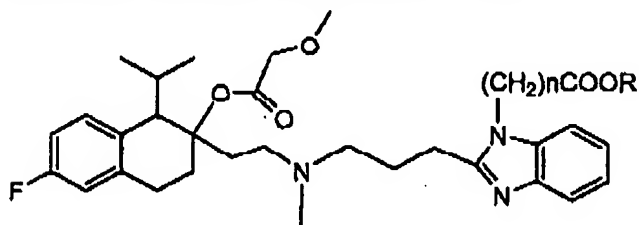
$R = \text{lower alkyl optionally substituted OH or } NH_2$;



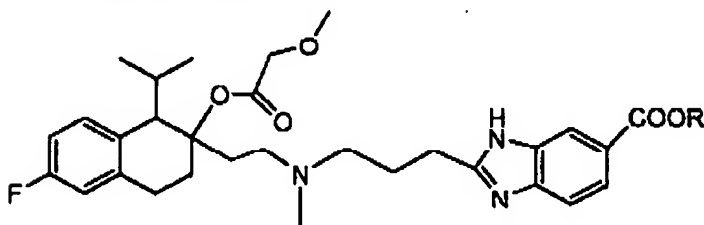
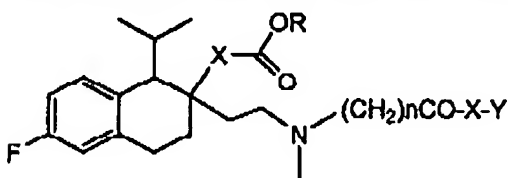
$R = \text{lower alkyl optionally substituted by OH or } NH_2$;



n=1 to 3

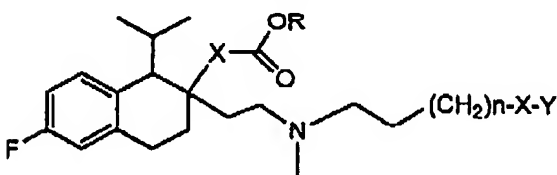
R=lower alkyl optionally substituted by OH or NH₂;

n=1 to 3

R=lower alkyl optionally substituted by OH or NH₂;R=lower alkyl optionally substituted by OH or NH₂;

n=1 to 3 X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl; and

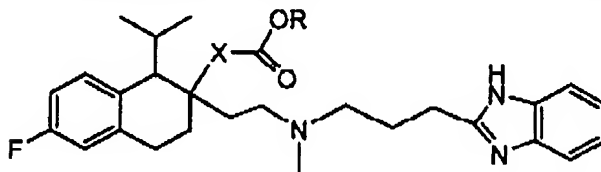


n=0 to 2

X=O, S, SO, SO₂, NH NR or N(CH₂)_mCOOH where m is 0 or 2

Y=aryl or heterocyclyl substituted with (CH₂)_mCOOH where m is 0 to 2.

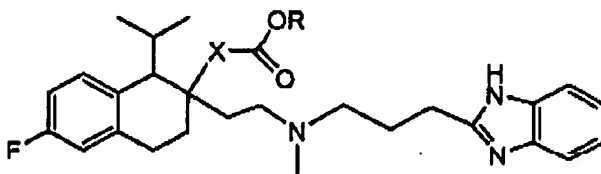
4. (Withdrawn) The compound, according to claim 3, having the following structure:



X=bond, CH₂, or OCH₂

R=lower alkyl optionally substituted OH or NH₂.

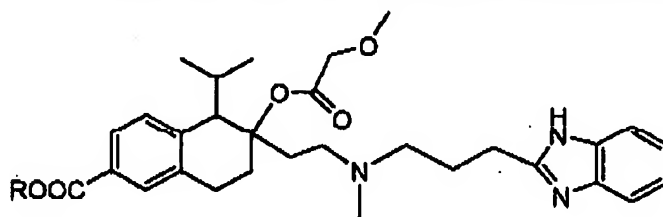
5. (Withdrawn) The compound, according to claim 3, having the following structure:



X=bond, CH₂, or OCH₂

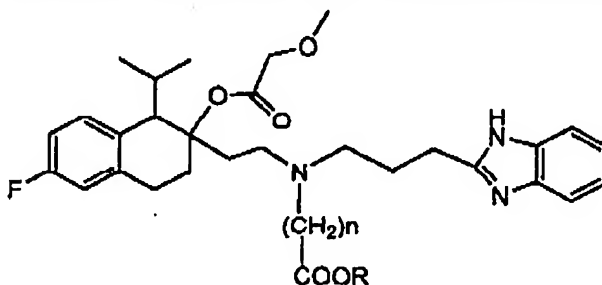
R=lower alkyl optionally substituted OH or NH₂.

6. (Withdrawn) The compound, according to claim 3, having the following structure:



R=lower alkyl optionally substituted by OH or NH₂.

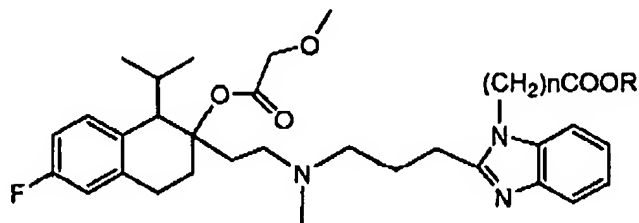
7. (Withdrawn) The compound, according to claim 3, having the following structure:



n=1 to 3

R=lower alkyl optionally substituted by OH or NH₂.

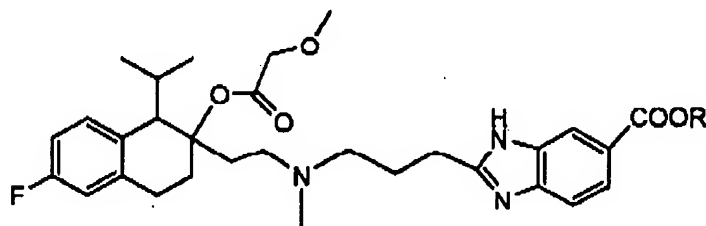
8. (Withdrawn) The compound, according to claim 3, having the following structure:



n=1 to 3

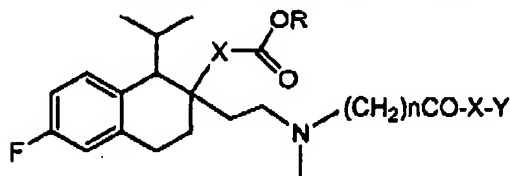
R=lower alkyl optionally substituted by OH or NH₂.

9. (Withdrawn) The compound, according to claim 3, having the following structure:



R=lower alkyl optionally substituted by OH or NH₂.

10. (Withdrawn) The compound, according to claim 3, having the following structure:

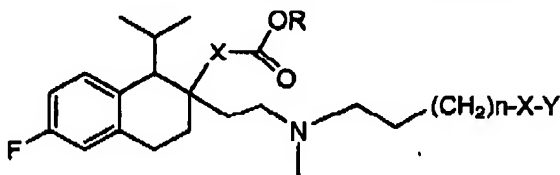


n=1 to 3

X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl.

11. (Withdrawn) The compound, according to claim 3, having the following structure:



n=0 to 2

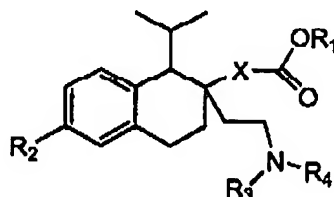
X=O, S, SO, SO₂, NH NR or N(CH₂)_mCOOH where m is 0 or 2

Y=aryl or heterocyclyl substituted with $(CH_2)_mCOOH$ where m is 0 to 2.

12. (Withdrawn) A pharmaceutical composition comprising a calcium channel blocker compound having at least one of the following characteristics:

- a. the compound is metabolized both by CYP450 and by a non-oxidative metabolic enzyme or system of enzymes;
- b. the compound has a short (up to four (4) hours) non-oxidative metabolic half-life;
- c. the compound contains a hydrolysable bond that can be cleaved non-oxidatively by hydrolytic enzymes;
- d. the primary metabolites of the compound result from the non-oxidative metabolism of the compound;
- e. the primary metabolites are soluble in water at physiological pH;
- f. the primary metabolites have negligible inhibitory activity at the IK_R (HERG) channel at normal therapeutic concentration of the parent drug in plasma;
- g. the compound, as well as the metabolites thereof, does not cause metabolic DDJ when co-administered with other drugs; and
- h. the compound, as well as metabolites thereof, does not elevate LFT values when administered alone; wherein said composition further comprises a pharmaceutical carrier.

13. (Withdrawn) The pharmaceutical composition, according to claim 12, wherein said compound has the following structure:



wherein:

X=a bond, $(CH_2)_n$, O, S, or $O(CH_2)_n$,

wherein n=1-6;

$R_1=C_{1-6}$ alkyl, optionally substituted with OH or NH_2 ;

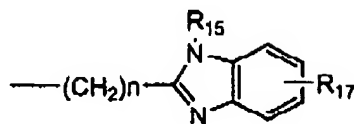
$R_2=F$ or $COOR_5$,

wherein R_5 is C_{1-6} alkyl, optionally substituted with OH or NH_2 ;

$R_3=CH_2$ or $(CH_2)_n-COOR_6$,

wherein n=1-6 and R_6 is C_{1-6} alkyl, optionally substituted with OH or NH_2 ;

$R_4=(CH_2)_n-COR_7R_8$, $-(CH_2)_n-R_{10}R_{11}$ or



$R_7 = O, NH, \text{ or } NR_9,$

$R_8 = \text{optionally substituted aryl or heterocycle,}$

$R_9 = C_{1-6} \text{ alkyl,}$

$R_{10} = O, S, SO, SO_2, NH, \text{ or } NR_{12} \text{ or } N(CH_2)_mCOOR_{13},$

$R_{11} = \text{aryl or heterocyclyl optionally substituted with } (CH_2)_nCOOR_{14},$

$R_{12} = C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2,$

$R_{13} = C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2,$

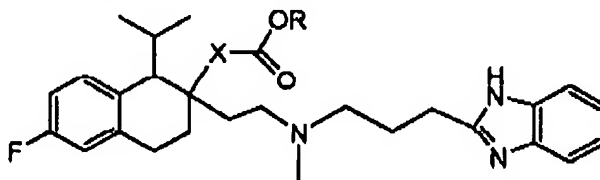
$R_{14} = C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2,$

$R_{15} = (CH_2)_nCOOR_{16},$

$R_{16} = C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2,$

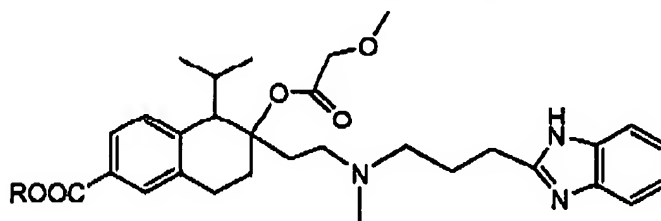
$R_{17} = \text{not present or } COOR_{18} \text{ wherein } R_{18} \text{ is } C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2, \text{ and}$
 wherein $n = 1-6$.

14. (Withdrawn) The composition, according to claim 13, comprising a compound having a formula selected from the group consisting of:

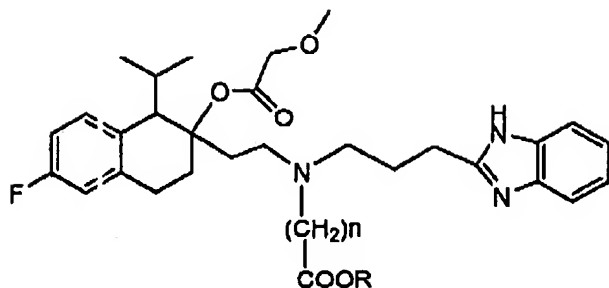


$X = \text{bond, } CH_2, \text{ or } OCH_2$

$R = \text{lower alkyl optionally substituted OH or } NH_2;$

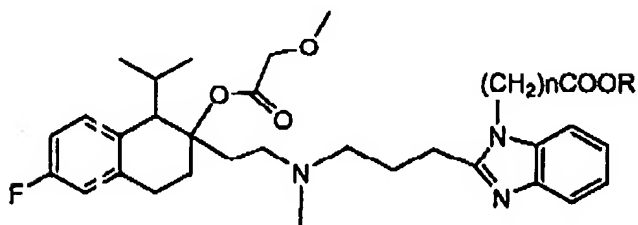


$R = \text{lower alkyl optionally substituted by OH or } NH_2;$



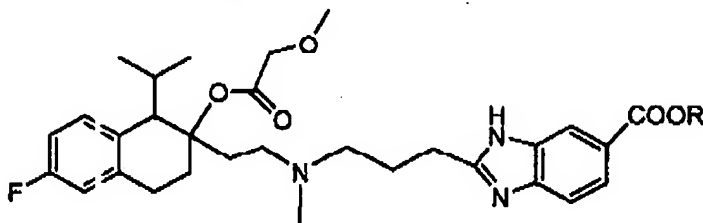
$n=1$ to 3

R=lower alkyl optionally substituted by OH or NH₂;

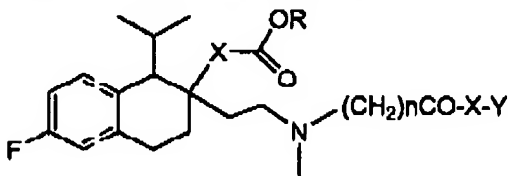


$n=1$ to 3

R=lower alkyl optionally substituted by OH or NH₂;

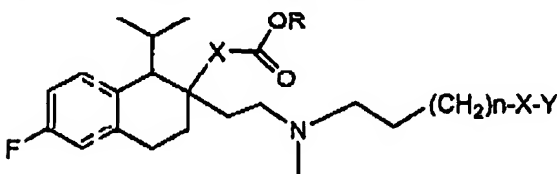


R=lower alkyl optionally substituted by OH or NH₂;



$n=1$ to 3 X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl; and

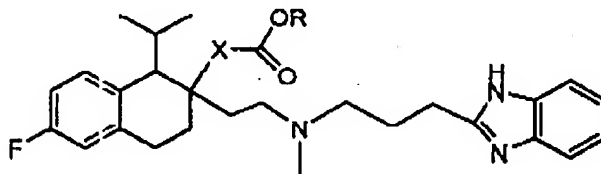


$n=0$ to 2

X=O, S, SO , SO_2 , NH NR or $\text{N}(\text{CH}_2)_m\text{COOH}$ where m is 0 or 2

Y=aryl or heterocyclyl substituted with $(\text{CH}_2)_m\text{COOH}$ where m is 0 to 2.

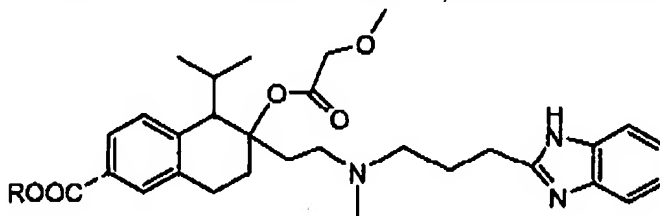
15. (Withdrawn) The compound, according to claim 14, comprising a compound having the following structure:



X=bond, CH_2 , or OCH_2

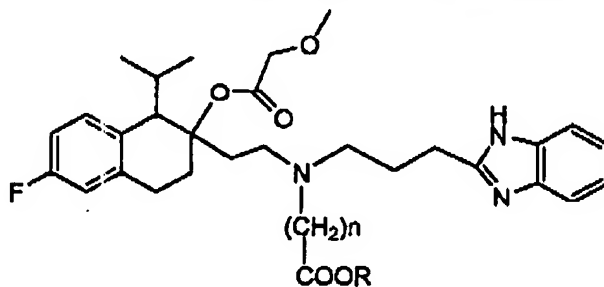
R=lower alkyl optionally substituted OH or NH_2 .

16. (Withdrawn) The compound, according to claim 14, having the following structure:



R=lower alkyl optionally substituted by OH or NH_2 .

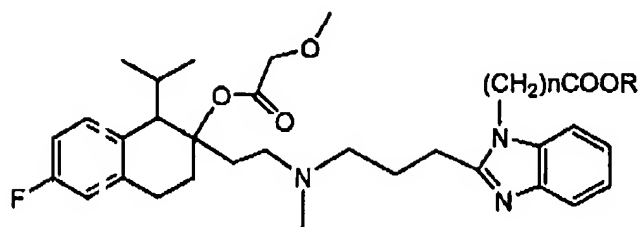
17. (Withdrawn) The compound, according to claim 14, having the following structure:



n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2 .

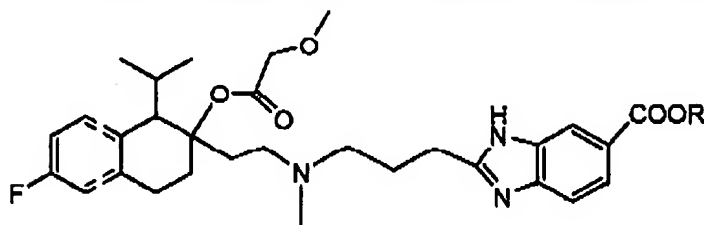
18. (Withdrawn) The compound, according to claim 14, having the following structure:



$n=1$ to 3

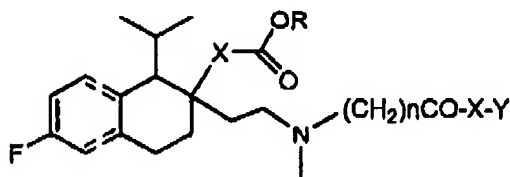
R=lower alkyl optionally substituted by OH or NH₂.

19. (Withdrawn) The compound, according to claim 14, having the following structure:



R=lower alkyl optionally substituted by OH or NH₂.

20. (Withdrawn) The compound, according to claim 14, having the following structure:

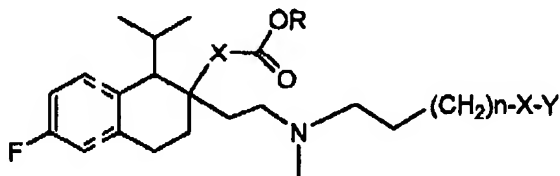


$n=1$ to 3

X=O, NH NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl.

21. (Withdrawn) The compound, according to claim 14, having the following structure:



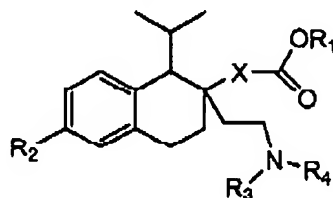
$n=0$ to 2

X=O, S, SO₂, NH NR or N(CH₂)_mCOOH where m is 0 or 2

Y=aryl or heterocyclyl substituted with (CH₂)_mCOOH where m is 0 to 2.

22. (Canceled)

23. (Currently Amended) ~~The method, according to claim 22, A method for blocking a calcium channel in a patient in need of such blocking wherein said method comprises administering to said patient a calcium channel blocking compound wherein said compound has the following structure:~~



wherein:

X=a bond, (CH₂)_n, O, S, or O(CH₂)_n,

wherein n=1-6;

R₁=C₁₋₆ alkyl, optionally substituted with OH or NH₂;

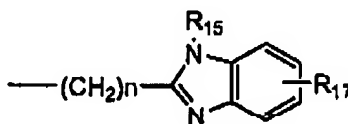
R₂=F or COOR₅,

wherein R₅ is C₁₋₆ alkyl, optionally substituted with OH or NH₂;

R₃=CH₃ or (CH₂)_n-COOR₆,

wherein n=1-6 and R₆ is C₁₋₆ alkyl, optionally substituted with OH or NH₂;

R₄=(CH₂)_n-COR₇R₈, -(CH₂)_n-R₁₀R₁₁ or



R₇=O, NH, or NR₉,

R₈=optionally substituted aryl or heterocycle,

R₉=C₁₋₆ alkyl,

R₁₀=O, S, SO, SO₂, NH, or NR₁₂ or N(CH₂)_mCOOR₁₃,

R₁₁=aryl or heterocyclyl optionally substituted with (CH₂)_nCOOR₁₄,

R₁₂=C₁₋₆ alkyl, optionally substituted with OH or NH₂,

R₁₃=C₁₋₆ alkyl, optionally substituted with OH or NH₂,

R₁₄=C₁₋₆ alkyl, optionally substituted with OH or NH₂,

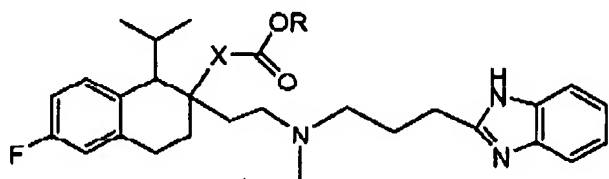
R₁₅=(CH₂)_nCOOR₁₆,

R₁₆=C₁₋₆ alkyl, optionally substituted with OH or NH₂,

R₁₇=not present or COOR₁₁ wherein R₁₈ is C₁₋₆ alkyl, optionally substituted with OH or NH₂, and

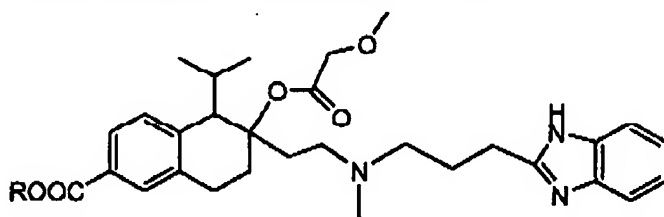
wherein n=1-6.

24. (Currently Amended) ~~The method, according to claim 23, A method for blocking a calcium channel in a patient in need of such blocking wherein said method comprises administering to said patient a calcium channel blocking compound wherein said compound has a formula selected from the group consisting of:~~

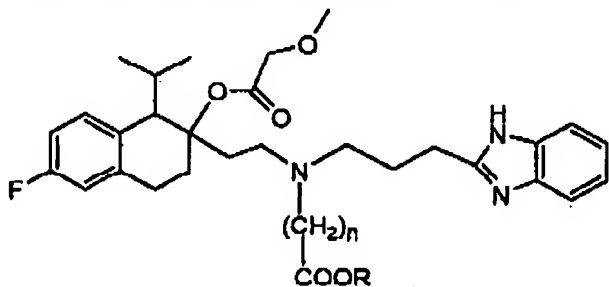


X=bond, CH₂, or OCH₂

R=lower alkyl optionally substituted OH or NH₂;

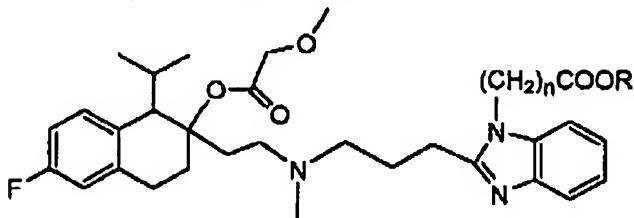


R=lower alkyl optionally substituted by OH or NH₂;



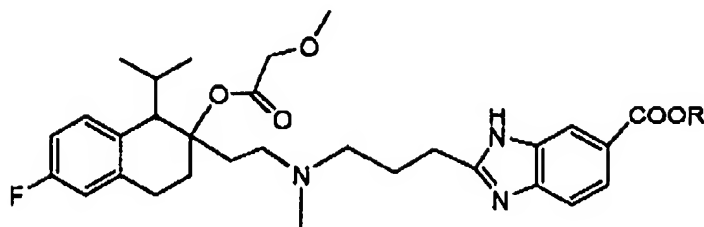
n=1 to 3

R=lower alkyl optionally substituted by OH or NH₂;

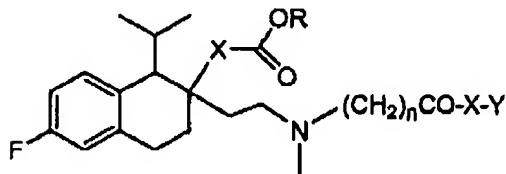


n=1 to 3

R=lower alkyl optionally substituted by OH or NH₂;

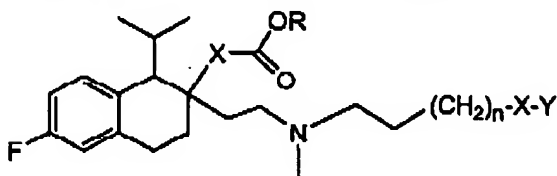


R=lower alkyl optionally substituted by OH or NH₂;



n=1 to 3 X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl; and

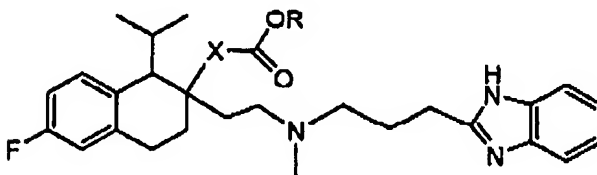


n=0 to 2

X=O, S, SO, SO₂, NH NR or N(CH₂)_mCOOH where m is 0 or 2

Y=aryl or heterocyclyl substituted with (CH₂)_mCOOH where m is 0 to 2.

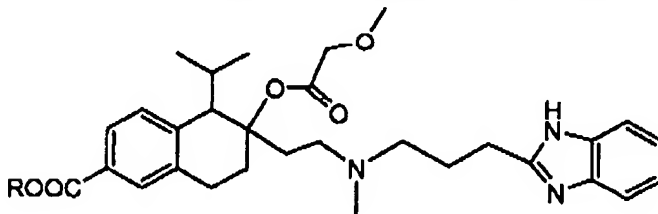
25. (Original) The compound, according to claim 24, wherein said compound has the following structure:



X=bond, CH₂, or OCH₂

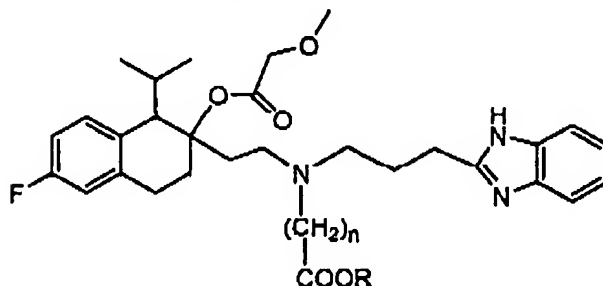
R=lower alkyl optionally substituted OH or NH₂.

26. (Original) The compound, according to claim 24, wherein said compound has the following structure:



R=lower alkyl optionally substituted by OH or NH₂.

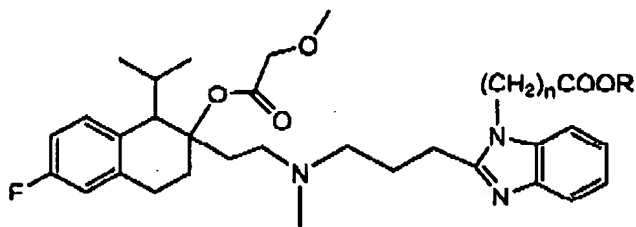
27. (Original) The compound, according to claim 24, wherein said compound has the following structure:



n=1 to 3

R=lower alkyl optionally substituted by OH or NH₂.

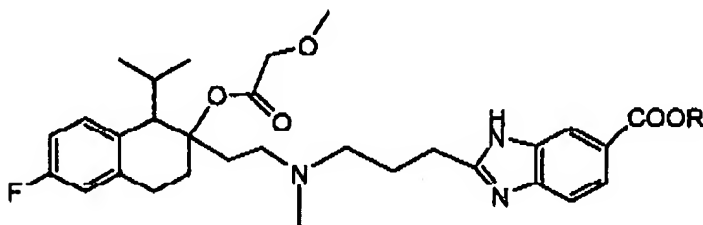
28. (Original) The compound, according to claim 24, wherein said compound has the following structure:



n=1 to 3

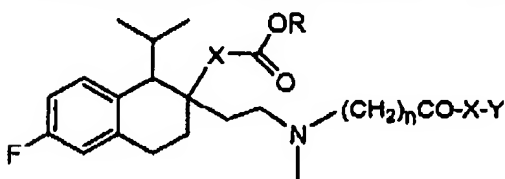
R=lower alkyl optionally substituted by OH or NH₂.

29. (Original) The compound, according to claim 24, wherein said compound has the following structure:



R=lower alkyl optionally substituted by OH or NH₂.

30. (Withdrawn) The compound, according to claim 24, wherein said compound has the following structure:

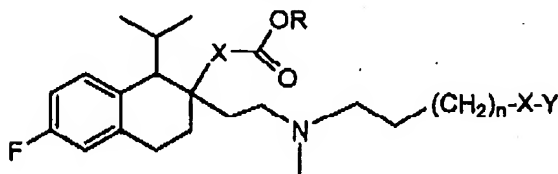


n=1 to 3

X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl.

31. (Withdrawn) The compound, according to claim 24, wherein said compound has the following structure:



n=0 to 2

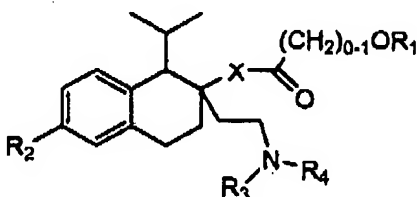
X=O, S, SO, SO₂, NH NR or N(CH₂)_mCOOH where m is 0 or 2

Y=aryl or heterocyclyl substituted with (CH₂)_mCOOH where m is 0 to 2.

32. (Currently Amended) The method, according to claim-2223, wherein the patient is a human.

33. (Currently Amended) The method, according to claim 2223, wherein said method is used to treat a condition selected from the group consisting of hypertension, angina, ischemia, arrhythmia, congestive heart failure, and cardiac insufficiency.

34. (New) A method for blocking a calcium channel in a patient in need of such blocking wherein said method comprises administering to said patient a calcium channel blocking compound wherein said compound has the following structure:



wherein:

X=a bond, (CH₂)_n, O, S, or O(CH₂)_n,

wherein n=1-6;

R₁=C₁₋₆ alkyl, optionally substituted with OH or NH₂;

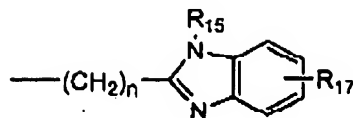
R₂=F or COOR₅,

wherein R₅ is C₁₋₆ alkyl, optionally substituted with OH or NH₂;

R₃=CH₃ or (CH₂)_n-COOR₆,

wherein n=1-6 and R₆ is C₁₋₆ alkyl, optionally substituted with OH or NH₂;

R₄=(CH₂)_n-COR₇R₈, -(CH₂)_n-R₁₀R₁₁ or



$R_7 = O, NH, \text{ or } NR_9,$

$R_8 = \text{optionally substituted aryl or heterocycle,}$

$R_9 = C_{1-6} \text{ alkyl,}$

$R_{10} = O, S, SO, SO_2, NH, \text{ or } NR_{12},$

$R_{11} = \text{aryl or heterocyclyl optionally substituted with } (CH_2)_n COOR_{14},$

$R_{12} = C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2,$

$R_{13} = C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2,$

$R_{14} = C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2,$

$R_{15} = \text{is H,}$

$R_{17} = \text{not present or } COOR_{18} \text{ wherein } R_{18} \text{ is } C_{1-6} \text{ alkyl, optionally substituted with OH or } NH_2, \text{ and}$
wherein $n = 1-6.$